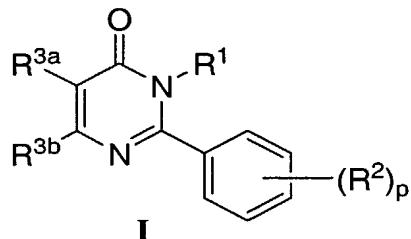


WHAT IS CLAIMED IS:

1. A compound of Formula I:



5 or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

a is 0 or 1;

b is 0 or 1;

m is 0, 1 or 2;

10 p is 1 to 3;

r is 0 or 1;

s is 0 or 1;

R¹ is selected from:

15 1) H,

2) C₁-C₁₀ alkyl,

3) aryl,

4) C₂-C₁₀ alkenyl,

5) C₂-C₁₀ alkynyl,

20 6) C₁-C₆ perfluoroalkyl,

7) C₁-C₆ aralkyl,

8) C₃-C₈ cycloalkyl, and

9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R⁴;

R² is independently selected from:

1) (C=O)_aO_bC₁-C₁₀ alkyl,

2) (C=O)_aO_baryl,

- 3) $(C=O)_aObC_2-C_{10}$ alkenyl,
- 4) $(C=O)_aObC_2-C_{10}$ alkynyl,
- 5) CO_2H ,
- 6) halo,
- 7) OH ,
- 8) ObC_1-C_6 perfluoroalkyl,
- 9) $(C=O)_aNR^6R^7$,
- 10) CN ,
- 11) $(C=O)_aObC_3-C_8$ cycloalkyl,
- 12) $(C=O)_aOb$ heterocyclyl,
- 13) $SO_2NR^6R^7$, and
- 14) $SO_2C_1-C_{10}$ alkyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more substituents selected from R⁴;

R^{3a} and R^{3b} are independently selected from:

- 1) H ,
- 2) $(C=O)_aObC_1-C_{10}$ alkyl,
- 3) $(C=O)_aOb$ aryl,
- 4) $(C=O)_aObC_2-C_{10}$ alkenyl,
- 5) $(C=O)_aObC_2-C_{10}$ alkynyl,
- 6) CO_2H ,
- 7) halo,
- 8) OH ,
- 9) ObC_1-C_6 perfluoroalkyl,
- 10) $(C=O)_aNR^6R^7$,
- 11) CN ,
- 12) $(C=O)_aObC_3-C_8$ cycloalkyl,
- 13) $(C=O)_aOb$ heterocyclyl,
- 14) $SO_2NR^6R^7$, and
- 15) $SO_2C_1-C_{10}$ alkyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more substituents selected from R⁴;

R⁴ is independently selected from:

- 1) $(C=O)_a O_b C_1-C_{10}$ alkyl,
- 2) $(C=O)_a O_b$ aryl,
- 3) C_2-C_{10} alkenyl,
- 4) C_2-C_{10} alkynyl,
- 5) $(C=O)_a O_b$ heterocyclyl,
- 6) CO_2H ,
- 7) halo,
- 8) CN ,
- 9) OH ,
- 10) $O_b C_1-C_6$ perfluoroalkyl,
- 11) $O_a (C=O)_b NR^6 R^7$,
- 12) oxo,
- 13) CHO ,
- 14) $(N=O)R^6 R^7$,
- 15) $(C=O)_a O_b C_3-C_8$ cycloalkyl,
- 16) $SO_2 NR^6 R^7$, and
- 17) $SO_2 C_1-C_{10}$ alkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R⁵;

20

R⁵ is selected from:

- 1) $(C=O)_r Os(C_1-C_{10})$ alkyl,
- 2) $O_r (C_1-C_3)$ perfluoroalkyl,
- 3) (C_0-C_6) alkylene- $S(O)_m R^a$,
- 25) 4) oxo,
- 5) OH ,
- 6) halo,
- 7) CN ,
- 8) $(C=O)_r Os(C_2-C_{10})$ alkenyl,
- 30) 9) $(C=O)_r Os(C_2-C_{10})$ alkynyl,
- 10) $(C=O)_r Os(C_3-C_6)$ cycloalkyl,
- 11) $(C=O)_r Os(C_0-C_6)$ alkylene-aryl,
- 12) $(C=O)_r Os(C_0-C_6)$ alkylene-heterocyclyl,
- 13) $(C=O)_r Os(C_0-C_6)$ alkylene- $N(R^b)_2$,
- 35) 14) $C(O)R^a$,

- 15) $(C_0\text{-}C_6)\text{alkylene-CO}_2R^a$,
- 16) $C(O)H$,
- 17) $(C_0\text{-}C_6)\text{alkylene-CO}_2H$, and
- 18) $C(O)N(R^b)_2$,

5 said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH , $(C_1\text{-}C_6)\text{alkoxy}$, halogen, CO_2H , CN , $O(C=O)C_1\text{-}C_6$ alkyl, oxo, and $N(R^b)_2$;

R^6 and R^7 are independently selected from:

- 10 1) H ,
- 2) $(C=O)ObC_1\text{-}C_{10}$ alkyl,
- 3) $(C=O)ObC_3\text{-}C_8$ cycloalkyl,
- 4) $(C=O)Obaryl$,
- 5) $(C=O)Obheterocyclyl$,
- 15 6) $C_1\text{-}C_{10}$ alkyl,
- 7) aryl,
- 8) $C_2\text{-}C_{10}$ alkenyl,
- 9) $C_2\text{-}C_{10}$ alkynyl,
- 10) heterocyclyl,
- 20 11) $C_3\text{-}C_8$ cycloalkyl,
- 12) SO_2R^a , and
- 13) $(C=O)NR^b_2$,

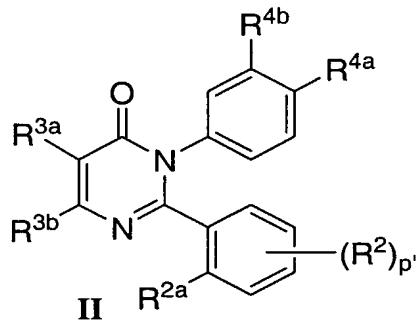
said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^6 , or

25 R^6 and R^7 can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^5 ;

R^a is $(C_1\text{-}C_6)\text{alkyl}$, $(C_3\text{-}C_6)\text{cycloalkyl}$, aryl, or heterocyclyl; and

R^b is H , $(C_1\text{-}C_6)\text{alkyl}$, $(C_1\text{-}C_6)\text{alkyl-NR}^a_2$, $(C_1\text{-}C_6)\text{alkyl-NH}_2$, $(C_1\text{-}C_6)\text{alkyl-NHR}^a$, aryl, heterocyclyl, $(C_3\text{-}C_6)\text{cycloalkyl}$, $(C=O)OC_1\text{-}C_6$ alkyl, $(C=O)C_1\text{-}C_6$ alkyl or $S(O)R^a$.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, of the Formula II:



5 wherein a, b, r, s, R⁴, R⁵, R⁶ and R⁷ are defined as in Claim 1 for the compound of the Formula I and

p' is 0 to 2;

10 R² is selected from:

- 1) (C=O)_aC₁-C₁₀ alkyl,
- 2) (C=O)_aaryl,
- 3) (C=O)_aNR⁶R⁷,
- 4) (C=O)_aC₃-C₈ cycloalkyl,
- 15 5) (C=O)_aheterocyclyl,
- 6) SO₂NR⁶R⁷, and
- 7) SO₂C₁-C₁₀ alkyl,

said alkyl, aryl, cycloalkyl, and heterocyclyl is optionally substituted with one or more substituents selected from R⁴;

20 R^{2a} is selected from: halogen and (C₁-C₆)alkyl;

R^{3a} and R^{3b} are independently selected from: hydrogen, (C₁-C₆)alkyl, trifluoromethyl and halogen; and

25 R^{4a} and R^{4b} are independently selected from: hydrogen, halogen and (C₁-C₆)alkyl, provided that at least one is not hydrogen, or

R^{4a} and R^{4b} are combined to form a diradical selected from -CH₂CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH=CH-O- and -CH=CH-N-.

5 3. The compound according to Claim 2 or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

wherein:

10 p' is 0 to 2;

 r is 0 or 1;

 s is 0 or 1;

15 R² is (C₁-C₆)alkylene-NR⁶R⁷; said alkylene is optionally substituted with up to three substituents selected from OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and NR⁶R⁷;

R^{2a} is selected from: halogen and (C₁-C₆)alkyl;

20 R^{3a} and R^{3b} are independently selected from: hydrogen, (C₁-C₆)alkyl, trifluoromethyl and halogen;

25 R^{4a} and R^{4b} are independently selected from: hydrogen, halogen and (C₁-C₆)alkyl, provided that at least one is not hydrogen;

R⁵ is selected from:

- 1) (C=O)_rOs(C₁-C₁₀)alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,
- 3) (C₀-C₆)alkylene-S(O)_mR^a,

30 4) oxo,

5) OH,

6) halo,

7) CN,

8) (C=O)_rOs(C₂-C₁₀)alkenyl,

35 9) (C=O)_rOs(C₂-C₁₀)alkynyl,

- 10) $(C=O)_r Os(C_3-C_6)$ cycloalkyl,
- 11) $(C=O)_r Os(C_0-C_6)$ alkylene-aryl,
- 12) $(C=O)_r Os(C_0-C_6)$ alkylene-heterocyclyl,
- 13) $(C=O)_r Os(C_0-C_6)$ alkylene- $N(R^b)_2$,
- 5 14) $C(O)R^a$,
- 15) (C_0-C_6) alkylene- CO_2R^a ,
- 16) $C(O)H$,
- 17) (C_0-C_6) alkylene- CO_2H , and
- 18) $C(O)N(R^b)_2$,

10 said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, (C_1-C_6) alkoxy, halogen, CO_2H , CN, $O(C=O)C_1-C_6$ alkyl, oxo, and $N(R^b)_2$;

R6 and R7 are independently selected from:

- 15 1) H,
- 2) C_1-C_{10} alkyl,
- 3) aryl,
- 4) heterocyclyl,
- 5) C_2-C_{10} alkenyl,
- 20 6) C_2-C_{10} alkynyl, and
- 7) C_3-C_8 cycloalkyl,

said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^5 , or

25 R6 and R7 can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^5 ;

30 R^a is (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, aryl, or heterocyclyl; and

R^b is H, (C_1-C_6) alkyl, (C_1-C_6) alkyl- NR^a_2 , (C_1-C_6) alkyl- NH_2 , (C_1-C_6) alkyl- NHR^a , aryl, heterocyclyl, (C_3-C_6) cycloalkyl, $(C=O)OC_1-C_6$ alkyl, $(C=O)C_1-C_6$ alkyl or $S(O)_2R^a$.

35 4. A compound which is

2-(2-bromophenyl)-3-(3-fluoro-4-methylphenyl)pyrimidin-4(3H)-one.

5. A pharmaceutical composition that is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

6. A pharmaceutical composition that is comprised of a compound in accordance with Claim 3 and a pharmaceutically acceptable carrier.

10 7. A method of treating or preventing cancer in a mammal in need of such treatment that is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1.

15 8. A method of treating or preventing cancer in a mammal in need of such treatment that is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 3.

20 9. A method of treating cancer or preventing cancer in accordance with Claim 7 wherein the cancer is selected from cancers of the brain, genitourinary tract, lymphatic system, stomach, larynx and lung.

25 10. A method of treating or preventing cancer in accordance with Claim 7 wherein the cancer is selected from histiocytic lymphoma, lung adenocarcinoma, small cell lung cancers, pancreatic cancer, glioblastomas and breast carcinoma.

11. A process for making a pharmaceutical composition which comprises combining a compound of Claim 1 with a pharmaceutically acceptable carrier.

30 12. The composition of Claim 5 further comprising a second compound selected from: an estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonist, a PPAR- δ agonist; an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle 35 checkpoint, and an apoptosis inducing agent.

5 13. The composition of Claim 12, wherein the second compound is an angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-(chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin, troponin-1, and an antibody to VEGF.

10 14. The composition according to Claim 12 further comprising a proteosome inhibitor.

15 15. The composition according to Claim 12 further comprising a aurora kinase inhibitor.

16. The composition according to Claim 12 further comprising a Raf kinase inhibitor.

20 17. The composition according to Claim 12 further comprising a serine/threonine kinase inhibitor.

18. The composition according to Claim 12 further comprising an inhibitor of another mitotic kinesin which is not KSP.

25 19. The composition of Claim 12, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

30 20. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

35 21. A method of treating or preventing cancer that comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a compound selected from: an estrogen receptor modulator, an androgen receptor modulator, retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase

inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonist, a PPAR- δ agonist, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

22. A method of treating cancer that comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy and a compound selected from: an estrogen receptor modulator, an androgen receptor modulator, retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonist, a PPAR- δ agonist, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

23. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

24. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.

25. The method of Claim 24 wherein the GPIIb/IIIa antagonist is tirofiban.

26. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.

27. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a proteosome inhibitor.

28. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an aurora kinase inhibitor.

5 29. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a Raf kinase inhibitor.

10 30. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a serine/threonine kinase inhibitor.

15 31. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an inhibitor of a mitotic kinesin that is not KSP.

32. A method of modulating mitotic spindle formation which comprises administering a therapeutically effective amount of a compound of Claim 1.

20 33. A method of inhibiting the mitotic kinesin KSP which comprises administering a therapeutically effective amount of a compound of Claim 1.